IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	) Examiner: Daniel M. Sullivan
Van Der Kooy et al.	) Art Unit: 1636
Serial No. 09/966,768	)
Filed: September 28, 2001	)
For: "Primitive Neural Stem Cells)	
and Method for	)
Differentiation of Stem	)
Cells to Neural Cells"	)

DECLARATION OF DEREK VAN DER KOOY

I, Derek van der Kooy, declare:

1. I am a named inventor of the subject matter claimed in United States Patent Application No. 09/966,768, filed on September 28, 2001 (hereinafter the '768 application).

2. I attended the University of Toronto where I obtained a Ph.D. in 1980 in the area of anatomy. I am currently a Professor at the University of Toronto. My education and professional experience are described in further detail in my curriculum vitae, a copy of which was provided with my declaration dated March 8, 2006 that was previously submitted in the '768 application on March 10, 2006.

3. I have read and understood the Office Action, dated August 10, 2005 in the '768 application and the response filed on February 10, 2006. The purpose of this declaration is to provide factual evidence that primitive neural stem cells can be generated from embryonic stem cells in the absence of leukemia inhibitory factor (LIF) by the methods provided in the '768 application.

4. Amended claims 1, 20, 33, 35, 37, and 47 submitted with the February 10, 2006 response state that the media "optionally" comprises LIF. The response identifies portions of the '768 application that do not require the serum-free media to contain LIF.

5. The specification of the '768 application discloses culture conditions and methods to generate primitive neural stem cells. Differentiation of human embryonic stem ("HES") cells into primitive neural stem cells can be performed in the presence or absence of LIF.

6. The "HES-Derived Neurospheres" graph attached as Appendix A shows derivation of human neurospheres clonally in the absence of LIF. Primary neurospheres were derived from HES cells grown at clonal densities (10 cells/µl). The value obtained with the Lif,EFH,B27 sample (i.e., HES cultured in media comprising LIF, B27 and EFH (E= epidermal growth factor (EGF), F=fibroblast growth factor (FGF), H=heparin)) is 1.5 spheres per 3000 cells while the non-LIF sample named EFH,B27 produced a value of 0.375 spheres per 3000 cells. Thus, while the frequency of neurosphere generation appears greater with LIF, neurospheres are still obtained without LIF as indicated in the '768 application.

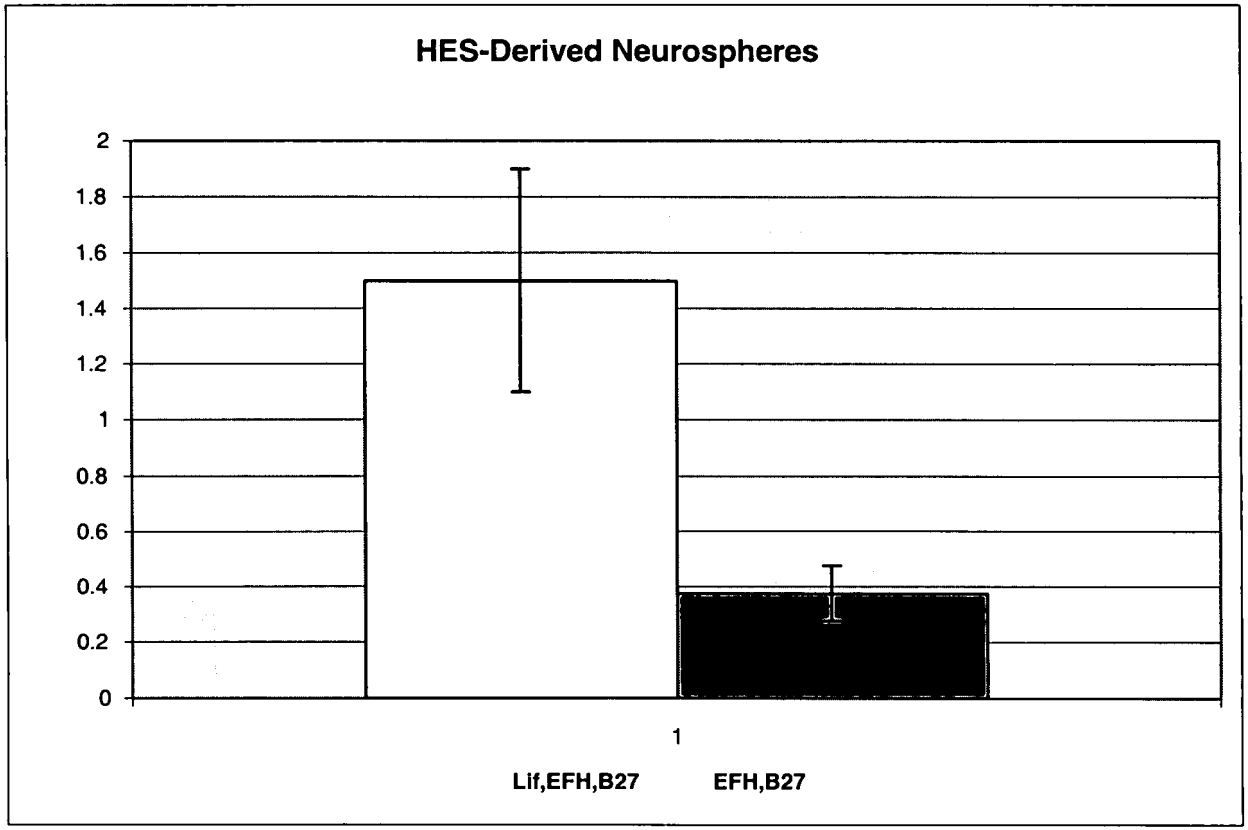
7. The data described above clearly demonstrates the successful isolation of human primitive neural stem cells in the presence or absence of LIF. This data shows that LIF is optional for production of human primitive neural stem cells.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Respectfully submitted,

Date: March 31/06

Derek van der Kooy



Appendix A